

### **IN THE CLAIMS**

Please **cancel** claims 5-12, 16-23, and 25-40 without prejudice or disclaimer. Applicants reserve the right to recapture any unclaimed subject matter in any subsequently filed divisional applications.

Please **amend** the claims 1, 3-4, 13-15, and 24 as follows:

1. (Twice Amended) A human-compatible monoclonal antibody which is specific for human CD28 and activates human T-lymphocytes of several to all sub-groups without being artificially crosslinked with a secondary antibody and without occupancy of an antigen receptor of the human T-lymphocytes and thus antigen-non-specifically, and which is effective for treating a disease with pathologically reduced number of CD4 T-cells or an autoimmune disease.
3. (Twice Amended) A monoclonal antibody according to claim 1, with the hybridoma cells enabled to produce monoclonal human-CD28 specific animal antibodies being available through
  - a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-I-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
  - b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
  - c) cultivation of the transfected cells received in b) above,
  - d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
  - e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
  - f) removal of spleen cells of the mice immunized in this way and fusing the spleen cells with cells of the cell line X63-Ag 8.653 by means of

- polyethylene glycol to produce the hybridoma cells,
- g) selection of the hybridoma cells produced in f) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind on human CD28 expressing mouse A20J and/or L929 cells, and
- h) cultivation/sub-cloning of the selected hybridoma cells obtained in g) above and isolating the monoclonal antibodies.

4. (Amended) A hybridoma cell for the production of a monoclonal antibody according to claim 1, which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the SalI-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) above and fusing the spleen cells with cells of the cell line X63-Ag 8.653 by means of polyethylene glycol, and
- g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind on human CD28 expressing mouse A20J and/or L929 cells.

13. (Amended) A monoclonal antibody according to claim 2, enabled to produce monoclonal human-CD28 specific animal antibodies being available through

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the SalI-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) above and fusing the spleen cells with cells of the cell line X63-Ag 8.653 by means of polyethylene glycol to produce the hybridoma cells,
- g) selection of the hybridoma cells received as in f) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells, and
- h) cultivation/sub-cloning of the selected hybridoma cells obtained in g) above and isolating of the antibodies therefrom.

14. (Amended) A hybridoma cell for the production of a monoclonal antibody according to claim 2 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the SalI-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,

- b) fusing the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized in this way and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
- g) selection of the hybridoma cells received as in e) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.

15. (Amended) A hybridoma cell for the production of a monoclonal antibody according to claim 3 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-I-neo vector following excision of the SalI-HindIII fragment and production of protoplasts from *Escherichia coli* (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,

- f) removal of spleen cells of the mice immunized as in e) above and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
- g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.

24. (Amended) A hybridoma cell for the production of a monoclonal antibody according to claim 13 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
- g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.